REMARKS

I. Introduction

In response to the Office Action dated October 29, 2004, claims 44-46 have been amended. Claims 31, 36, 37, 39 and 43-48 remain in the application. Entry of these amendments, and reconsideration of the application, as amended, is requested.

II. Claim Amendments

Applicants' attorney has amended claims 44-46 to clarify that the composition is a pharmaceutical composition. These amendments are made solely for the purpose of clarifying the language of the claims. Entry of these amendments is respectfully requested.

III. Restriction Requirement

Applicants acknowledge that the restriction requirement was made final in the April 14, 2004 Office Action. At page 2 of the Office Action dated October 29, 2004, the Examiner asserted that claims 36-37, 39, 43-45 and 47-48 are drawn to a nonelected invention. This assertion is believed to be in error. Applicant has attempted to bring this issue to the Examiner's attention in each response and via telephone to no avail. The Examiner is respectfully requested to read the following and respond so that the record can be clarified.

First, the restriction requirement that was raised in the Office Action dated July 28, 2003, restricted claims 31, 34 and 36-50 into 110 groups. The groups were defined as the synthetic oligonucleotides having the nucleotide sequences of TGACGTCA and SEQ ID NO: 1-4 and 6-110. Applicants were required to elect one of the 110 sequences for prosecution. As acknowledged by the Examiner, Applicants responded by electing SEQ ID NO: 10.

Applicants note further that the originally filed application included claims 1-25, directed to synthetic oligonucleotides as well as methods. A restriction requirement dated July 19, 2001, restricted the application to one of four groups, three of which groups were directed to method claims and one of which group encompassed the synthetic oligonucleotide claims. Applicants elected the synthetic oligonucleotide group and prosecution continued to the point of identification of allowable claims before the application was assigned to a new examiner. The new and current Examiner issued subsequent restriction requirements that required restriction within the original

single group of synthetic oligonucleotides. Yet none of the subsequent further restrictions required restriction among different claims relating to the same, single nucleotide sequence elected by Applicants.

Moreover, Applicants believe the Examiner has overlooked the amendment to the claims made in the response dated August 16, 2004. At that time Applicants' attorney amended claims 31, 37 and 39 to delete reference to non-elected subject matter. In addition, claims 36, 37, 39, 44, 45, 47 and 48 were amended to update the references to previous claims in view of the cancellation of claims 34 and 41.

No basis has yet to be provided by the Patent Office for excluding claim 43 from the current examination directed to claims 31 and 46.

Applicants urge the Examiner to reconsider the restriction requirement and rejoin the withdrawn claims. Each and every one of the currently pending claims is limited to the synthetic oligonucleotide of SEQ ID NO: 10.

The Examiner stated in item 3 of page 2 of the outstanding Office Action that a "complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action". Applicants respectfully note that none of the pending claims is directed to nonelected subject matter.

IV. Prior Art Rejections

In paragraphs (5)-(8) of the Office Action, claims 31 and 46 were rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Flynn et al., Biochemistry 1996, Vol. 35, pages 7308-7315 (Flynn) and Billing-Medel et al., U.S. Patent No. 6,183,952 (Billing).

Applicants respectfully traverse this rejection.

The prior art rejection relies on an assertion that the combined teachings of Flynn and Billing render the subject matter of claims 31 and 46 obvious. As discussed at page 5 of Applicants' response dated August 16, 2004, this assertion is based on erroneous assumptions.

At page 3 of the outstanding Office Action, the Examiner states, in "response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references." Applicants do not dispute the Examiner's statement. Applicants' arguments did not merely attack the

references individually. Instead, the teachings of each reference were summarized in order to make the point that neither reference provides the motivation or suggestion to arrive at the claimed invention.

At page 3 of the outstanding Office Action, the Examiner asserts that the "prior art teaches links between the instant CpG dinucleotide and tumor development and thus provides sufficient motivation to combine the oligonucleotide of Flynn with a pharmaceutically acceptable carrier such as water." This statement is not true. The Examiner has not pointed to a teaching, in Flynn or elsewhere, that the claimed oligonucleotide is linked to tumor development. Even if it were true that Flynn taught a link between the oligonucleotide of SEQ ID NO: 10 and tumor development, that would not suffice to provide a motivation to modify the oligonucleotide of SEQ ID NO: 10 to incorporate phosphorothioate linkages or to add a pharmaceutically acceptable carrier, unless it was known that this alleged link between the oligonucleotide and tumor development involved an inhibitory effect of the oligonucleotide on tumor development.

The portion of Flynn cited by the Examiner to support the assertion that Flynn (or other prior art) teaches a link between the CpG dinucleotide of the invention and tumor development is the following statement at column 2 of page 7308 of Flynn: "The anticancer agent 5-azadeoxycytidine functions by inhibiting the DCMTase (Jutterman et al., 1994), and DCMTase activity contributes substantially to tumor development in a mouse model of intestinal neoplasia (Laird et al., 1995)." This statement supports the assertion that an agent known to inhibit DCMTase is likely to be useful in the treatment of tumor development and cancer. It says nothing about whether the substrates listed in Table 1 can be used as inhibitors of DCMTase or as anti-cancer agents.

The key point that has not been addressed by the Patent Office is that the prior art did not teach or suggest that the synthetic oligonucleotide having the nucleotide sequence shown in SEQ ID NO: 10 and recited in Applicants' claims is an inhibitor of DCMTase or otherwise is useful as an anti-cancer agent. It appears the Examiner may be assuming that, because the substrates listed in Table 1 of Flynn "were designed to mimic DNA transcriptional cis elements previously reported to have cytosine C-5 methylated regulation," this suffices to teach that each of these substrates can be used not only as a substrate for DCMTase, but also as an inhibitor of DCMTase activity. Yet, as

V. Conclusion

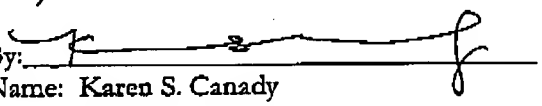
In view of the above, it is submitted that this application is now in good order for allowance and such allowance is respectfully solicited. Should the Examiner believe minor matters still remain that can be resolved in a telephone interview, the Examiner is urged to call Applicants' undersigned attorney.

Respectfully submitted,

GATES & COOPER LLP
Attorneys for Applicant(s)

Howard Hughes Center
6701 Center Drive West, Suite 1050
Los Angeles, California 90045
(310) 641-8797

Date: December 29, 2004

By: 
Name: Karen S. Canady
Reg. No.: 39,927

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evidenced by Applicants' data (see Fig. 1B), not all substrates listed in Table 1 of Flynn have this inhibitory activity on DCMTase (see CRE a^{mct}).

The Examiner appears to be confusing "substrate" of DCMTase with "inhibitor" of DCMTase. Those skilled in the art, however, would not consider any substrate of DCMTase to be useful as an anti-cancer or other therapeutic agent. Accordingly, those skilled in the art would not be motivated to modify the synthetic oligonucleotide of GC-box b^{mct} in Table 1 of Flynn to introduce phosphorothioate linkages or to add a pharmaceutically acceptable carrier.

At page 4 of the Office Action, the Examiner asserts that Billing provides sufficient motivation to introduce phosphorothioate linkages into the substrates of Flynn. This is based on the teaching in Billing that antisense oligonucleotides act with greater efficacy when modified to contain artificial internucleotide linkages such as phosphorothioate linkages. Yet the Examiner has not stated where in the prior art it is taught that the synthetic oligonucleotide of Applicants' claims is useful as an antisense oligonucleotide. Flynn does not teach or suggest the use of the substrates listed in Table 1 therein as antisense oligonucleotides.

The Examiner is respectfully requested to reconsider and withdraw the rejections based on the prior art in view of these arguments. Should the Examiner maintain his previous position, explicit identification of the motivation in the prior art for arriving at the claimed invention would help to clarify issues for consideration on appeal. As indicated in a voicemail left with the Examiner, Applicants' undersigned representative would be most receptive to a telephone discussion to clarify these issues.

At page 4 of the Office Action, the Examiner added the comment that "claiming an unpatentable compound in combination with a carrier does not render the combination patentable." Applicants maintain that, without motivation to use a compound in a pharmaceutical context, there can be no motivation to combine the compound with a pharmaceutically acceptable carrier. To facilitate prosecution, however, Applicants are willing to clarify this intent by amending claims 44-46 to recite "pharmaceutical" to modify the word "composition". Should such an amendment not be helpful to furthering prosecution, the Examiner is authorized to refuse entry of the proposed amendment to claims 44-46.